

Appl. No. : 08/765,837
Filed : September 7, 1999

AMENDMENTS TO THE CLAIMS

1-30. Cancelled

31. (Currently amended) An isolated antigenic fragment of the human Factor VIII polypeptide of SEQ ID NO: 21, said fragment comprising at least 7 amino acids of a human Factor VIII fragment selected from the group consisting of a human Factor VIII fragment extending from arginine 1652 to arginine 1696 inclusive, a human Factor VIII fragment extending from threonine 1739 to tyrosine 1748 inclusive (SEQ ID NO: 3), a human Factor VIII fragment extending from asparagine 1777 to phenylalanine 1785 inclusive (SEQ ID NO: 4), and a human Factor VIII fragment extending from glutamic acid 1885 to arginine 1917 inclusive.

32. (Currently Amended) The isolated antigenic polypeptide fragment according to Claim 31, wherein said human Factor VIII fragment comprises an epitope selected from the up consisting of: a human Factor VIII fragment extending from arginine 1652 to tyrosine 1664 (SEQ ID No: 1), a human Factor VIII fragment extending from threonine 1739 to tyrosine 1748 (SEQ ID No: 3), a human Factor VIII fragment extending from asparagine 1777 to phenylalanine 1785 (SEQ ID No: 4), a human Factor VIII fragment extending from glutamic acid 1885 to phenylalanine 1891 (SEQ ID No: 7), a human Factor VIII fragment extending from glutamic acid 1893 to alanine 1901 (SEQ ID No: 8), and a human Factor VIII fragment extending from aspartic acid 1909 to arginine 1917 (SEQ ID No: 9).

33. (Currently amended) The isolated antigenic polypeptide fragment according to Claim 31, wherein said antigenic polypeptide comprises tyrosine or histidine.

34. (Currently Amended) An isolated conformational epitope comprising at least two different human Factor VIII fragments of Claim 32, wherein said fragments are positioned in proximity to each other when the protein is folded in its tertiary or quaternary structure to form a conformational epitope which is recognized by an inhibitor of Factor VIII selected from the group consisting of B lymphocytes, MHC I proteins, MHC II proteins, and anti-Factor VIII antibodies.

35. (Currently Amended) An isolated conformational epitope comprising at least two different epitopes from a fragment of the human Factor VIII polypeptide of SEQ ID NO: 21 wherein said fragment is selected from the group consisting of a human Factor VIII fragment extending from arginine 1652 to arginine 1696 inclusive, a human Factor VIII fragment

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extending from threonine 1739 to aspartic acid 1831, inclusive, and a human Factor VIII fragment extending from glutamic acid 1885 to arginine 1917 inclusive.

36. (**Currently Amended**) A complex, comprising a carrier protein or a carrier peptide linked to the polypeptide fragment of Claim 31 or the conformational epitope of Claim 35, wherein said complex has higher immunogenicity than said polypeptide of Claim 31.

37-38. (**Cancelled**)

39. (**Currently amended**) A pharmaceutical composition comprising at least the antigenic polypeptide fragment of Claim 31, or the conformational epitope of Claim 35 and an acceptable pharmaceutical vehicle.

40-43. (**Canceled**)

44. (**Previously presented**) The complex of Claim 36, wherein said carrier protein or said carrier peptide are bovine serum albumin or hemocyanin.

45. (**Currently amended**) An isolated polypeptide, consisting of a fragment of the human Factor VIII polypeptide of SEQ ID NO: 21, wherein said fragment is selected from the group consisting of a human Factor VIII fragment between arginine 1652 and arginine 1696 inclusive, ~~a human Factor VIII fragment between threonine 1739 and aspartic acid 1831 inclusive, and,~~ a human Factor VIII fragment between glutamic acid 1885 and arginine 1917 inclusive, and a fragment comprising at least 7 amino acids thereof, wherein said polypeptide is antigenic.

46. (**Previously presented**) A pharmaceutical composition, comprising the antigenic polypeptide of Claim 45 and an acceptable pharmaceutical vehicle.

47. (**Previously presented**) A complex, comprising a carrier protein or a carrier peptide linked to the antigenic polypeptide of Claim 45, wherein said complex has higher immunogenicity than said polypeptide of Claim 45.

48. (**Previously presented**) The complex of Claim 47, wherein said carrier protein or said carrier peptide are bovine serum albumin or hemocyanin.

49. (**Previously presented**) A conformational epitope comprising at least two different human Factor VIII fragments of Claim 45, wherein said fragments are positioned in proximity to each other when the protein is folded in its tertiary or quaternary structure to form a conformational epitope which is recognized by an inhibitor of Factor VIII selected from the

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group consisting of B lymphocytes, MHC I proteins, MHC II proteins, and anti-Factor VIII antibodies.

50. **(Currently amended)** An isolated ~~The~~ polypeptide according to Claim 45, consisting of a fragment of the human Factor VIII polypeptide of SEQ ID NO: 21, wherein said human Factor VIII fragment consists of an epitope selected from the group consisting of: a human Factor VIII fragment contained between arginine 1652 and tyrosine 1664 (SEQ ID No: 1), a human Factor VIII fragment contained between threonine 1739 and tyrosine 1748 (SEQ ID No: 3), a human Factor VIII fragment contained between asparagine 1777 and phenylalanine 1785 (SEQ ID No: 4), a human Factor VIII fragment contained between glutamic acid 1794 and tyrosine 1815 (SEQ ID No: 5), a human Factor VIII fragment contained between methionine 1823 and aspartic acid 1831 (SEQ ID No: 6), a human Factor VIII fragment contained between glutamic acid 1885 and phenylalanine 1891 (SEQ ID No: 7), a human Factor VIII fragment contained between glutamic acid 1893 and alanine 1901 (SEQ ID No: 8), and a human Factor VIII fragment contained between aspartic acid 1909 and arginine 1917 (SEQ ID No: 9), wherein said polypeptide is antigenic.

51. **(Previously presented)** A pharmaceutical composition, comprising the antigenic polypeptide of Claim 50 and an acceptable pharmaceutical vehicle.

52. **(Previously presented)** A complex, comprising a carrier protein or a carrier peptide linked to the antigenic polypeptide of Claim 50, wherein said complex has higher immunogenicity than said polypeptide of Claim 45.

53. **(Previously presented)** The complex of Claim 52, wherein said carrier protein or said carrier peptide are bovine serum albumin or hemocyanin.

54. **(Previously presented)** A conformational epitope comprising at least two different human Factor VIII fragments of Claim 50, wherein said fragments are positioned in proximity to each other when the protein is folded in its tertiary or quaternary structure to form a conformational epitope which is recognized by an inhibitor of Factor VIII selected from the group consisting of B lymphocytes, MHC I proteins, MHC II proteins, and anti-Factor VIII antibodies.

55. **(New)** An isolated polypeptide, consisting of a fragment of the human Factor VIII polypeptide of SEQ ID NO: 21, wherein said fragment is threonine 1739 to aspartic acid 1831, wherein said polypeptide is antigenic.

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SUMMARY OF INTERVIEW

Identification of Claims Discussed

Applicants thank the Examiner for extending the courtesy of a telephonic interview to Applicants' representatives on Feb. 2, 2004. During the interview, Claims 31-36, 39, 45-54, and new Claim 55 submitted herewith were discussed.

Proposed Amendments

The discussed amendments are incorporated into the section "**AMENDMENTS TO THE CLAIMS**" of the present Response to the Office Action.

Results of Interview

As provided in the Interview Summary mailed Feb. 5, 2004, the Examiner indicated that the Amendments submitted herewith would overcome all the remaining rejections. The Examiner also indicated that an updated search would be conducted prior to allowance.